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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	**PAPER NUMBER**
1644	8

DATE MAILED: 07/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/772938	HSUNG ET AL.
	Examiner	Art Unit
	GAMBEL	1644

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☑ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) _____ is/are pending in the application. 1-18

4a) Of the above claim(s) _____ is/are withdrawn from consideration. 4-8, 15, 18

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 1-3, 9-14, 16, 17

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☑ The translation of the foreign language provisional application has been received.

15)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☑ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

1. Applicant's amendment, filed 9/4/01 (Paper No. 17), has been entered.
Claims 42-56 have been canceled.
Claims 57-59 have been added.

2. Applicant's election of the combination of anti-CD40L antibody and anti-CD20 antibody and non-Hodgkin's disease as the B cell lymphoma in Paper No. 6, filed 4/11/02, is acknowledged.

Claims 1-3, 9-14 and 16-17 are under consideration in the instant application as they read on the elected species.

Claims 4-8, 15 and 18 have been withdrawn from consideration by the examiner, as being drawn to nonelected species.

3. No information disclosure statement has been filed with this application.

4. Formal drawings have been submitted which fail to comply with 37 CFR 1.84.
Please see the form PTO-948 previously sent in Paper No. 5.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, MUST be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings MUST be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in ABANDONMENT of the application.

5. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required

6. Claim 11 is objected to because in ends in two periods (..).

Claim 16 is objected to because "radiolobel" should be "radiolabel".

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-3, 9-14 and 16-17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Kaminski et al. (U.S. Patent No. 6,287,537) AND/OR Anderson et al. (U.S. Patent No. 5,843,439) in view of Gruss et al. (Leukemia and Lymphoma 24: 393-422, 1997), Carbone et al. (Am. J. Pathol. 147: 912- 922, 1995), Black et al. (U.S. Patent No. 6,001,358), in view of standard chemotherapeutic treatments, including combination therapy of malignancies, including lymphomas known and practiced by the ordinary artisan at the time the invention was made, as acknowledged on pages 41-45 of the instant specification.

Kaminski et al. teach the use of anti-CD20 antibodies, including radiolabeled anti-CD20 antibodies (e.g. B1) in combination with other treatments to treat B cell malignancies, including non-Hodgkin's lymphoma (e.g. column 8, paragraph 1) (see entire document, Summary of the Invention and Detailed Description of the Invention). Kaminski et al. teach various modes of dosages and administration that were well known to those of skill in the art in the treatment of B cell malignancy (e.g. see columns 9-12 and Examples), encompassed by the claimed invention.

Anderson et al. teach the use of anti-CD20, including radiolabeled anti-CD20 antibodies (e.g. 2B8 in cooperative strategies to treat B cell malignancies, including non-Hodgkin's lymphoma (e.g. column 3, paragraph 2) (See entire document, including Background of the Invention, Summary of the Invention, Detailed Description of the Invention, Claims).

Therefore, the prior art taught combination therapy to various B cell malignancies, including B cell non-Hodgkin's lymphoma with CD20-specific antibodies at the time the invention was made. Providing radiotherapy and chemotherapy was known and routinely practiced at the time the invention was made in the treatment of non-Hodgkin's lymphomas at the time the invention was made.

The references do not teach the use of radiolabeled CD20-specific antibodies in combination with CD40L-specific antibodies.

Carbone et al. teach the expression of CD40 on B cell non-Hodgkin's lymphoma and CD40 ligand expressing cells T cells were detected within neoplastic follicles and surrounding areas via immunohistochemistry analysis (see entire document, particularly page 917; B-Cell NHL). Carbone et al. Also discuss the role such CD40 ligand expressing T cells on CD40 expressing B cell lymphoma proliferation (See Discussion, particularly page 920, column 1, paragraph 1).

Gruss et al. teach that CD40 is expressed on B cell lymphomas and that the CD40:CD40L pathway, including CD40L-expressing T cells, which are readily detectable around neoplastic B cells, enhance B cell activation and growth (see pages 404-405, B cell Lymphomas and Lymphoproliferative Disorders and Discussion). Gruss et al. teach that the anti-proliferative and pro-apoptotic effects of recombinant CD40L on high grade B-NHLs offer an appealing biologic approach for treatment of these neoplasms (page 405, column 1). While Gruss et al. disclose the art known formation of neutralizing anti-mouse antibodies as a limitation of antibody therapy (page 405, column 1, lines 24-27), such limitations have been long addressed by the use of recombinant antibodies such as humanized antibodies, known and practiced in the art for a decade (also, see Black et al. herein).

Therefore, the prior art of Carbone et al. and Gruss et al. taught the importance of CD40L-mediated interactions in B cell non-Hodgkin's lymphoma and clinical manifestations of lymphoma growth and therapeutic intervention. Also as pointed out above, Gruss et al. does teach that CD40:CD40L interactions are par of cellular activation and neoplastic tumor cell growth which would be useful for the therapeutic management of $CD40^+$ tumors (see page 404, column 1).

Gruss et al. does not teach the art known CD40L-specific antibody antagonists, including the antibody species encompassed by the claimed invention.

Black et al. teach the use of gp39/CD40L-specific antibodies, including recombinant antibodies and antibody fragments, to inhibit CD40:CD40L interactions or where gp39 inactivation and/or modulation of the gp39(CD40L)/CD40 interaction is desirable (e.g. column 11, lines 34-39 and column 14, lines 35-38). (see entire document, including Summary of the Invention and Detailed Description of the Invention). Black et al. teach the art known advantages of recombinant antibodies and antibody fragments as therapeutic agents (see Detailed Description of the Invention), given their decreased immunogenicity compared to their native murine antibody counterparts and ease of production and homogeneity.

The instant specification acknowledges standard chemotherapeutic treatments of leukemias, including combination therapy was known and practiced by the ordinary artisan at the time the invention was made (see pages 41-45 of the instant specification). Therefore, the chemotherapeutic agents including the alkylating agents employed in the claimed methods was obvious, given their standard use by the ordinary artisan at the time the invention was made.

Given the teachings of Kaminksi et al. to employ radiolabeled antibodies in combination with other treatments to treat leukemia as well as the acknowledgment by applicant that combination therapy was known and practiced in the art at the time the invention was made, one of ordinary skill in the art would have been motivated to treat B cell leukemia with a combination of therapies.

Given the expression of CD20 and CD40 and the ability of activation via CD20 and/or CD40, the ordinary artisan would have been motivated to target B cell non-Hodgkin's lymphoma directly with radiolabeled CD20-specific antibodies and to diminish activation of said B cell leukemia by blocking activation by CD40 ligand expressing T cells with CD40L-specific antibodies.

One of ordinary skill in the art would have employed non-radiolabeled CD40L-specific antibodies, given the expression of CD40L on normal activated T cells and the role of such CD40L on such T cells to stimulate CD40-expressing B cell lymphoma cells, as taught above.

Given the standard regimen of chemotherapy in leukemic patients and the teachings of Kaminski et al. to combine standard therapy with radiolabeled antibodies, one of ordinary skill in the art at the time the invention was made to employ multiple modalities to treat B cell lymphomas. Given the addition of non-radiolabeled CD40L-specific antibodies, the ordinary artisan would have been administering a less toxic therapeutic regimen, when compared to radiolabeled antibodies and chemotherapeutic agents.

One of ordinary skill in the art at the time the invention was made would have been motivated to select radiolabeled CD20-specific antibodies, non-radiolabeled CD40L-specific antibodies and standard chemotherapeutic to treat B cell lymphomas at the time the invention was made, given the teachings above. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

10. The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam,* 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman,* 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 1-3, 9-14 and 16-17 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over pending claims of copending applications USSNs 09/435,992 . Given the election in the instant case, the conflicting claims may or may not be identical, depending upon the invention(s) elected in these copending applications. The claims are not patentably distinct from each other because they appear to read on the same or nearly the same reagents to treat the same or nearly the same leukemias and lymphomas.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
July 1, 2002